Periarteritis Nodosa (Panarteritis Nodosa) with Report of Four Proven Cases

Ross Paull, M.D., *La Jolla*

Jones,[5] and Baker,[1] in 1942, well reviewed and summarized the literature dealing with periarteritis nodosa and provided such splendid bibliographies that elaborate repetition now seems superfluous and extravagant if not presumptuous. Accordingly, it is intended to attempt to limit this presentation to bare essentials, and to submit a few additional references and a few ideas for consideration.

Periarteritis is, as the name implies, an inflammatory condition of the smaller arteries and arterioles in any part or parts of the human and some several animals. Whether it is entitled to the distinction of being a disease entity in itself is under dispute and study. Many believe that the disorder is a form or phase of a condition embracing a group of disorders featured by peculiar lesions of the smaller arteries and arterioles. Some of the group are: scleroderma, dermatomyositis, disseminated lupus erythematosis, Libman-Sacks "disease," and the syndromes described by Friedberg and Gross; rheumatic fever and rheumatoid arthritis have been introduced as relatives; Thompson[16] suggests that possibly Loffler's syndrome should be included in the clan.

Periarteritis nodosa was first described by Von Rokitansky,[17] and Kussmaul and Maier.[7] Seventy-one years later, Ophuls,[11] in 1923, reviewed the literature and found but 70 references to the disease. Rothstein and Welt,[14] in 1933, found 195 reported cases; Motley,[10] in 1936, found 215; Boyd,[2] in December 1938, found 395; and Wilson and Alexander[19] found about 200 authenticated cases described from early 1940 through 1943.

The tremendous increase in the number of cases of periarteritis nodosa being reported is very stimulating and somewhat disquieting, the latter not because this highly fatal disease has already become commonly recognized, but because there is accumulating evidence indicating that the disorder may be induced by the administration of various agents, some of which are in common use in all specialties and subspecialties of medico-surgical practice. The various agents which might induce a state of hypersensitiveness, and through this periarteritis nodosa, include serums, vaccines, sulfonamides, histamine, tissue extracts, and so forth. Possibly thiouracil, gold salts and other substances should be included.

It is highly probable that some part of the increase in the number of cases of periarteritis nodosa being reported is due to: (1) increased alertness of the medical profession toward the diagnosis of the condition; (2) the expanded use of old and the adoption of new diagnostic procedures; (3) the increasing percentage of autopsies without which many of the cases would be disposed of with an incorrect diagnosis; and (4) an increased interest in reporting the proven cases.

The cause or causes of periarteritis nodosa are not yet determined. Those favoring an infectious etiology have accused the spirochete of syphilis, other spirochetes, viruses, streptococci, staphylococci, and bacilli. Reimann, Price, and Herbut,[12] in 1934, reported two cases of combined trichinosis and periarteritis nodosa and suggested the possibility that the latter might have been secondary to the former. Gruber,[4] in 1925, first reported the possibility or probability of periarteritis nodosa being a hypersensitivity reaction. Rich and Gregory[13] have produced rather convincing evidence to substantiate Gruber's contention. Wilson and Alexander,[19] in 1945, offered further evidence and with their article supplied an extensive bibliography listing many articles dealing with the relationship of hypersensitiveness and periarteritis nodosa. Webb,[18] in 1944, reported a case of periarteritis in a woman with toxemia of pregnancy and puerperal sepsis. It is quite probable that more than one of these schools of thought will eventually be able to prove their contention.

The inflammatory reaction in the arteries and arterioles leads to the production of miliary aneurysms and to the extreme reduction or occlusion of the lumen, with resultant changes in the tissues thus denied their blood supply. These tissue responses, single or combined, consist in part of inflammation, edema, hemorrhage, ischemia, infarction, necrosis, ulceration, perforation, and fibrosis. Inflammatory granulomatous changes have been described by Lindsay, Aggeler and Lucia[8] and others.

Middleton and McCarter,[9] in 1935, published an article dealing with the diagnosis of periarteritis nodosa. While the disease spares no sex or age, it does seem somewhat more common in the male and in the fourth and fifth decades. About 10-15 per cent of the cases reported have been in children. The disease may be fulminating, particularly in children, or insidious, progressive or intermittent. The usual course in the fatal cases (about 95 per cent), runs a matter of four to eight months, the longest published case running 12 years.

Since the arterial involvement may be mild or severe, localized, scattered, or generalized, fulminating or chronic, the symptoms, findings, and course will, of consequence, be most protean. No tissue and so no system is immune to the ravages of the disorder. The tendency for the condition to become generalized is so prominent that multiple, if not all, systems of the body usually become involved. Its extremely protean nature in itself may be one of the most revealing features in disclosing the identity

As a colonel, M.C., A.U.S., the author was assigned to Medical Service, Letterman General Hospital, San Francisco, during the time the reported cases were observed.

of the disease. Quite uniformly the patients have lassitude, malaise, chronic fatigue, easy fatigability, fever and a leukocytosis. Beyond this the symptoms and findings depend on the distribution and magnitude of the vascular involvement. Though none of the following are essential to the diagnosis of the condition, the rather sudden and otherwise unexplained development of them, especially if in combination, should make one very suspicious of periarteritis nodosa or one of the related disorders: (1) Asthma, especially in an older person and with an eosinophilia of 15 per cent or more; (2) evidence of renal disease; (3) arterial hypertension; (4) diabetes mellitus; (5) peripheral neuritis; (6) evidence of peripheral vascular disease; (7) cardiac disorder.

Some special studies, none of which are uniformly helpful, to consider in the approach to the problem are:

1. Biopsies. (The gastrocnemius usually is a fruitful source.)
2. Repeated differential leukocyte counts.

Wilson and Alexander[19] identified asthma in 18 per cent of 300 consecutive cases of periarteritis nodosa. Of the asthmatic cases, 95 per cent showed hypereosinophilia ranging from 11 to 84 per cent. Only six per cent of the non-asthmatic cases showed hypereosinophilia.

3. Urinary sediments.

Krupp[6] has reported finding in 14 of 21 cases of periarteritis and related disorders single urine specimens presenting red blood cells, red cell casts, oval fat bodies, fatty and waxy casts and, frequently, broad casts. Here, under one coverslip, are seen the elements characteristic of all three stages of glomerular nephritis, which are usually separated by years or decades. (It was Krupp, then assigned to the laboratory service, who, on examining the urine of Case 1, first considered the case to be one of periarteritis nodosa or one of the related disorders.)

4. Sigmoidoscopy.

Felsen[3] reported finding characteristic changes in the distal gut.

This article has been prepared with the view of reporting four hitherto unreported proven cases of periarteritis nodosa, three of which were diagnosed antemortem; with the desire to remind all branches of the medical profession of the possibility that part of the somewhat alarming, rapidly progressing increase in the number of cases of periarteritis nodosa being reported may be cases induced by the administration of serums, sulfonamides, tissue extracts, or any other substance to which the body may develop a state of hypersensitivity;[4,13,19] and to introduce for consideration the possibility that the yellow fever vaccine, some of which became contaminated with an icterogenic virus, may have been directly or indirectly responsible for the development of periarteritis nodosa in the four cases being reported.

The patients in all four of the cases herein reported were vaccinated against yellow fever about February or March 1942. The patient in the first case became ill about May 10, 1942. In this case one cannot prove the existence of hepatitis prior to the onset of symptoms considered to represent the onset of his periarteritis nodosa. Mild hepatitis has not been uncommon, however, and furthermore its coexistence might be masked by or blended with the periarteritis nodosa. In the second case, hepatitis with cholemia developed in mid-May, 1942, and the symptoms of his periarteritis about June 20, 1942. In the third case, hepatitis with cholemia developed in June, 1942. The patient never became asymptomatic therefrom so that it is difficult to localize temporally the onset of the manifestations of his periarteritis nodosa. However, a persisting unfavorable change in his condition developed in November, 1942. In the fourth case hepatitis with cholemia developed following yellow fever vaccination. This fourth case was not diagnosed antemortem, and as a consequence the date of the hepatitis was not obtained for the clinical record. While some of the periarteritis nodosa lesions in this fourth case were young, some were old enough to date back to at least the summer of 1942.

All four of the cases were Army officer patients admitted to Letterman General Hospital, an Army installation. Therefore, it might justifiably be contended that these officers, to develop periarteritis nodosa at all at the time they did, would have to develop it after having been vaccinated against yellow fever, for nearly everyone in the military service in that area had been so vaccinated early in 1942. It is highly probable that all these officers had received other vaccines about the same time, such as tetanus, triple typhoid, typhus, and less likely cholera and plague. These vaccines should be kept in mind as possible occasional offenders. The fact that all four were commissioned personnel may be partly explained by the tendency of the relative youthfulness of the enlisted personnel to make them less vulnerable.

In any event, this shower of four deaths from periarteritis nodosa in a single medical installation over a period of 26 months is no less than remarkable if not significant. The registrar of this installation, which has been in constant operation since about the turn of the century, informs me that as of January 15, 1946, these four cases are all they have ever had. There were 194 autopsies at this installation in this interval of 26 months. Periarteritis nodosa was the cause of death in four (2 per cent) of these cases. Webb[18] reported periarteritis nodosa as having been found in two of 1,510 consecutive autopsies at Freedmen's Hospital, Washington, D. C., from 1930 to 1944. Jones[5] reported 14 cases being admitted to the University Hospital of the University of Michigan between October 9, 1930, and November 4, 1940. This is a concentrated group, but the report does not include figures permitting one to calculate what per cent of total admissions or autopsies were cases of periarteritis nodosa. It may confidently be assumed that the 14 cases reported from the University of Michigan Hospital had not been vaccinated against yellow fever, but it may not be assumed they did not receive serum, sulfonamides, or other agents capable of sensitizing individuals. It is agreed that

the proposition that the yellow fever vaccine may have played a role in the induction of the disorder in these four cases is open to argument as well as consideration. An analysis of the natural deaths in the military services since early 1942 as compared to one for the three preceding years might be illuminating. For various obvious reasons, medical statistics from military installations cannot be effectively compared to those from civilian institutions.

Symptomatic and supportive treatment and the appropriate treatment of the extremely protean consequences of the vascular lesions seem about all that can yet be defended with much evidence.

CASE REPORTS

CASE NUMBER 1: A 44 year old white, male Army officer was hospitalized May 31, 1942, because of unexplained and progressive headaches, feverishness, fatigue, lassitude, general malaise and a sense of heaviness and soreness all over, but especially in his four extremities at and between his joints. In addition, he complained of anorexia, loss of interest in his hitherto relished tobacco, dark urine, ankle edema, tenderness in his calves, and pain in the calves aggravated by walking.

Prior to this illness the officer enjoyed an essentially unblemished health record. He had been vaccinated against yellow fever about February or March, 1942, but reported no unusual reaction therefrom.

The physical examination on hospitalization revealed moderate fever, tachycardia of 120 per minute, a slate colored skin, slight tenderness of the muscles of the thighs, moderate to marked tenderness of the muscles of the legs, and moderate pitting ankle edema.

Laboratory Findings: Urinalyses on admission revealed only mild proteinuria and 15 to 20 hyaline casts per H.P.F. Soon thereafter, red blood corpuscles appeared in abnormal numbers. Somewhat later, but before June 15, 1942, the urine sediments carried abnormal numbers of R.B.C. and W.B.C., fine hyaline, granular, cellular and R.B.C. casts, many R.B.C. and W.B.C. tubular casts and a few broad casts.

The blood Kahn was normal and the blood sedimentation rate on admission was normal; it was not repeated. The blood urea nitrogen gradually rose from an admission level of 10 mgm. per cent to 27 mgm. per cent by June 26; it had returned to about 15 mgm. per cent by July 31. Plasma proteins on two occasions in June were about 4.5 grams per 100 cc.; the A:G ratio was on each occasion 0.56. Intravenous phenolsulfonthalein, June 6, yielded 45 per cent in one hour and 60 per cent in two hours.

Thick smears of blood for malaria were normal and prostatic smears yielded only many gram positive cocci, while agglutinations for typhoid, paratyphoid A and B, undulant fever, and Proteus X-19 were normal. Blood cultures were sterile. The prothrombin time on June 27 was 25 seconds.

The E.C.G. on June 1 revealed only sinus tachycardia of 106, and x-ray films of bones, joints, lungs, heart and abdomen revealed no disease. The R.B.C. ranged between 3.3 and 4.4 million; the hemoglobin between 70 and 90 per cent; the W.B.C. 10 to 23 thousand and the eosinophils between 1 and 9 per cent.

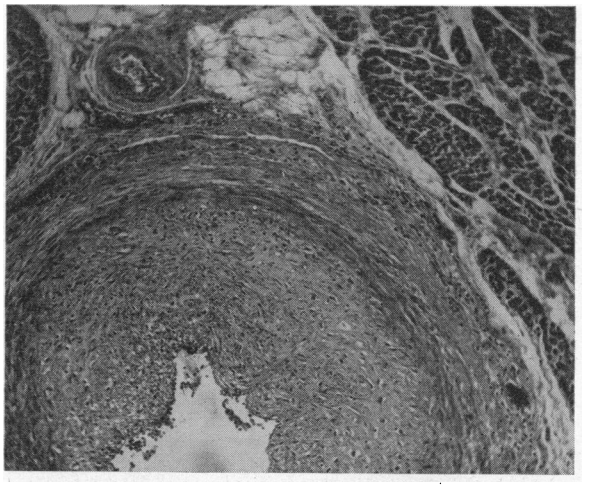
Biopsy of a section of gastrocnemius muscle, right median belly, taken two weeks after the patient was hospitalized, revealed microscopically typical pathology of periarteritis nodosa.

During the first week of hospitalization, the patient had a normal morning but high afternoon temperature, developed chills, episodes of profuse diaphoresis, and severe pains in both legs. These, with the admission symptoms, persisted until about mid-June, by which time he had developed, in addition, a paralysis of the dorsiflexors of both feet, and a constant fever. Characteristic urinary sediments were identified and reported by Krupp,[6] then assigned to the Laboratory Service, prior to the confirming biopsy from the gastrocnemius muscle June 15, 1942.

During the last two weeks of June, the patient was much relieved of all symptoms except the paralysis of the dorsiflexors of both feet. Thereafter, his course was a series of relapses and remissions of all symptoms except the paralysis, which was permanent. Early in July, atrophy, which proved to be progressive and became extreme, was noted in the musculature of all four extremities. About July 20, severe pains developed in both forearms. On August 15, he was delirious and combative. Such episodes became progressively more frequent and severe until his demise September 11, 1942. Treatment in this and the three cases to follow was symptomatic and supportive: low residue diet, anodynes, sedatives, transfusions, and so forth.

Clinical Diagnosis: Periarteritis Nodosa.

Anatomic Diagnoses: 1. Periarteritis Nodosa, generalized, severe; 2. Infarction, small intestine, multiple, severe, secondary to "1"; 3. Perforation, small intestine, complete, secondary to "1" and "2"; 4. Peritonitis, adhesive, chronic, extensive, severe, secondary to "1", "2" and "3".



CASE No. 1.—Coronary arteries showing degenerative changes of media, marked intimal thickening and proliferation, and infiltration of polymorphonuclears, lymphocytes, and occasional eosinophils throughout all layers.

CASE NUMBER 2: A 54 year old white, male Army officer was hospitalized July 1, 1942, because of fever, anorexia, malaise, episodes of profuse diaphoresis, polyuria, dark urine, grayish stools, aching pains in both legs aggravated by walking or prolonged standing, and a small blotchy erythematous rash which started on his legs and gradually spread to his arms and back.

Except for arterial hypertension of some 15 years' standing and "swollen ankles" toward evening for an indefinite but extended period ending some several weeks before his current illness, and a period of anorexia, nausea, heaviness in the region of the liver, and jaundice in May, 1942, the patient had enjoyed good health. With the exception of the jaundice, the symptoms which developed in May, 1942, persisted to or fused with the present illness. He had been vaccinated against yellow fever in February, 1942.

The admission physical examination revealed: A Raynaud-like syndrome in all manual digits, prominent mottling of

the skin of both legs, a mild tachycardia, fever of 100° F., blood pressure of 175/95, the left lobe of the prostate to be slightly enlarged, mild bilateral deafness, an arcus senilis, bilateral mild pitting edema of the ankles, and bilateral moderate tenderness of the calves.

As Case No. 1 with a very similar story and picture had been admitted to the same ward only a month earlier, it was very natural that periarteritis nodosa immediately was seriously considered and prominently listed in the working diagnosis.

Multiple urine studies revealed little or no protein; and inconstantly a few small R.B.C., hyaline, cellular, granular and waxy casts, but no broad casts. Blood Kahn was negative. The blood urea nitrogen values were within normal limits, while the serum proteins measured 5.2 grams for each 100 cc. (Albumin/globulin ratio 1:1.) A prostatic smear contained pus cells but no bacteria. Serum agglutinated E. typhi up to 1:1280 on July 4, 1942, and again on July 6, 1942. Blood and urine cultures were negative for all growths, and feces cultures were negative for typhoid group and no parasites or ova were found.

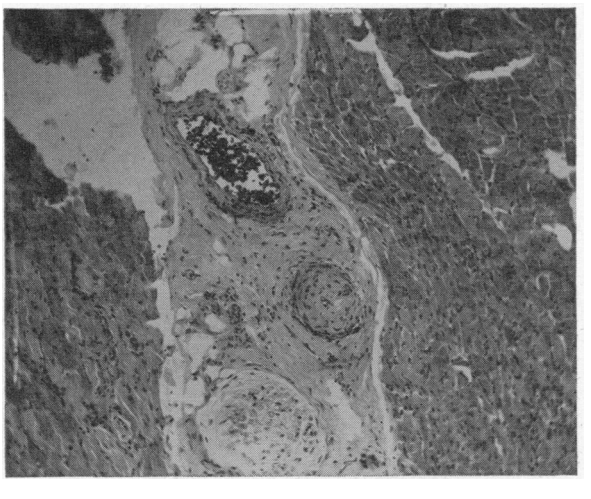
The icterus index varied from 11 to 34 units.

An electrocardiogram revealed sinus tachycardia and left axis deviation.

Biopsy of the right gastrocnemius muscle revealed diagnosis compatible with periarteritis nodosa.

Blood:	R.B.C.	W.B.C.	Hb.	Eosinophiles
7- 2-42	4.25	10400	90	Ranged from 1 to 4%
7-14-42	4.15	32000	90	
8- 1-42	3.67	21600	75	

During the first two weeks of hospitalization, the patient's condition was unchanged. Then the fingertips changed color from pallor to syanosis, the right foot became anesthetic, paresis of the dorsiflexors of the left hand and wrist developed, and the urine sediments began to resemble those so suggestive of periarteritis nodosa. On July 19 the patient wakened with a total paralysis of the extensors of the right wrist; on July 31 the paresis of the left wrist became a paralysis. On August 4 a biopsy from the gastrocnemius muscle confirmed the diagnosis. During August dry gangrene of the second left toe, both thumbs, and right middle finger developed, and there was extreme muscular atrophy of all four extremities. The patient rapidly failed and expired September 16, 1942.



CASE No. 2.—Muscle biopsy showing fibrosis of arterial wall with almost complete occlusion, and residual perivascular infiltrate of lymphocytes, polymorphonuclears, and occasional eosinophils. Note degenerative changes in skeletal muscle with altered staining reaction and marked sarcolemmal proliferation.

Clinical Diagnosis: 1. Periarteritis Nodosa.

Anatomic Diagnoses: 1. Periarteritis Nodosa, generalized, severe; 2. Infarction, myocardial, multiple, extensive, recent and old, secondary to "1"; 3. Perforation, small bowel and gall bladder, secondary to "1"; 4. Peritonitis, suppurative, acute, severe, secondary to "1" and "3"; 5. Infarction, with necrosis, pancreas, severe, secondary to "1".

CASE NUMBER 3: A 53 year old white, male medical officer was hospitalized March 2, 1943. The history of previous illnesses was noncontributory. In March, 1942, the patient was vaccinated against yellow fever. In June, 1942, at approximately the same time that others vaccinated with him developed hepatitis with cholemia, he developed anorexia, nausea, belching, gaseous abdominal distention, but, he thought, no jaundice. He was very tired. While indigestion disappeared after several weeks, the chronic fatigue and easy fatigability seemed progressive. About late November, 1942, pain in the calves developed, and this was aggravated by walking or prolonged standing. Through the course of the next three months these pains became more severe and gradually were accompanied by the same symptom in the thighs, back, shoulders, neck and arms. These pains seemed worse in the afternoon and evening. During the same three months prior to admission, chilly sensations and profuse night sweats gradually developed. In spite of all these symptoms, the patient had remained on duty until two weeks prior to admission, when he accepted sick-in-quarters status.

Physical examination upon admission revealed blood pressure of 115/75, a pulse rate of 88, a slight fever, slight tenderness at the left costovertebral angle and tenderness of both calves. A series of blood studies (R.B.C., W.B.C., Hb., and differential) showed normalcy except for a leukocytosis ranging between 10,000 and 20,000. Cultures of urine, blood and stools were normal, as were agglutinations for all the usual disease considered in chronic febrile disorders (except for typhoid and paratyphoid, in which cases the result was that to be expected in vaccinated military personnel). An electrocardiogram also was normal.

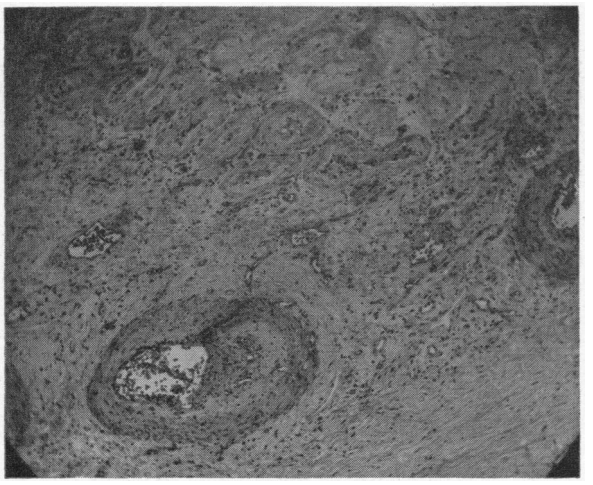
A series of urinalyses showed inconstant proteinuria without a significant number of R.B.C., W.B.C., or casts. Erythrocyte sedimentation rate was constantly rapid. X-ray films of the chest and heart, gastrointestinal tract, gall bladder and soft tissue of the legs all were normal, as were the pyelogram and a barium enema study. The blood Kahn also was normal. A biopsy specimen from the gastrocnemius showed periarteritis nodosa.

At about the time of hospitalization, the patient developed gaseous abdominal distention which thereafter was only partially relieved by enemas and prostigmine. All other symptoms became progressively worse until he died. Late in March he developed neuritic pains in all four extremities. Had the ward officer had the advantage of having seen Cases 1 and 2, he ought by then have grown very suspicious that he was dealing with another case of periarteritis nodosa. When the neuritic pains developed, Clarence Godard, Lt. Col., M. C., A. U. S., Chief of the Neuropsychiatric Service, was called in consultation. It was his opinion April 4, confirmed by biopsy the following day, that the patient had severe, multiple peripheral neuritis, probably secondary to periarteritis nodosa. About April 17 both feet became paralyzed and the right hand and wrist paretic.

At his own request and that of a physician friend, the patient received two courses of sulfadiazine, neither of which seemed to have favorable or unfavorable influence.

He progressively failed and on June 9 was unconscious, incontinent, pallid, and diaphoretic with shallow, slow, stertorous respiration, a weak, thready pulse, and a blood pressure of 60/40. He died that day.

Clinical Diagnosis: Periarteritis Nodosa.



CASE No. 3.—Testis showing organization and recanalization of thrombus in medium sized artery, with infiltration of all coats by polymorphonuclears, lymphocytes, and occasional eosinophils; the interstitial tissue is scarred and the tubules degenerated. In areas this testis showed acute infarction.

Anatomic Diagnoses: 1. Periarteritis Nodosa, generalized, severe; 2. Hemorrhage, multiple, of brain and pons, secondary to "1"; 3. Infarction, myocardial, acute, secondary to "1".

CASE NUMBER 4: A 64 year old white, male officer was hospitalized October 24, 1944, because of a recurrence or partial persistence of frequency, nocturia, and dysuria dating from about 1930. A transurethral prostatic resection had been done in December, 1943, and this had resulted in comfort which continued until late July, 1944.

About 1940 the patient had noticed an increase in ease of fatigability and mild pain in his left chest unrelated to exertion. An electrocardiogram taken at that time and another in June, 1942, he believed, were reported as being slightly abnormal. In June of 1943 he developed increased fatigability, lassitude, and dyspnea on slight exertion. The exertion also caused a pain in his left chest which sometimes radiated to his left upper arm. This was a sensation of fullness or pressure with an occasional sharp quality. The pains usually lasted from a few seconds to a minute and were relieved by rest. He had been vaccinated against yellow fever in February or March of 1942 and had developed hepatitis with cholemia a matter of two to four months thereafter.

Upon physical examination admission revealed blood pressure of 175/105, bilateral absence of dorsalis pedis pulsation, and uniformly smooth third degree enlargement of the prostate. The author saw this patient in consultation October 31, 1944, and was unable to get a history of any symptoms, except those referable to the urinary tract, prior to December of 1943 when the circulatory symptoms developed. However, an electrocardiogram dated June, 1943, was available, a fact which suggested there might have been symptoms then which had been the reason for taking the electrocardiogram. This record and one taken in December, 1943 revealed changes suggesting coronary insufficiency. The author found nothing additional in the way of physical changes.

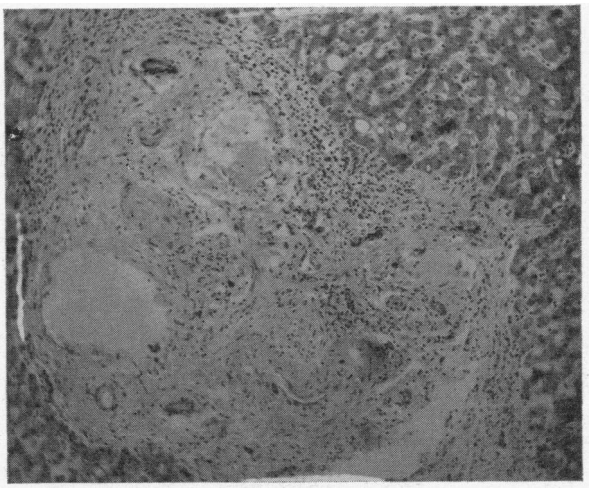
Recent, current studies, including an x-ray film of the heart and lungs, routine complete blood count and hemoglobin estimation, complete urinalysis, blood sugar, blood urea nitrogen, blood cholesterol, blood chloride, and electrocardiogram, showed no abnormality. In the light of these findings, the author gave the opinion that, should clotting, bleeding, and prothrombin times be normal (and they proved to be normal), the patient was a reasonably good surgical risk for a transurethral resection under sacral block anesthesia. In view of his circulatory history and transient electrocardiogram changes, it was recommended preoperative atropin and barbiturates be administered and that a plentiful supply of compatible blood be immediately available.

With these precautions, the transurethral resection was performed November 2, 1944. While it was anticipated that the patient would be in the operating room for an hour or less, severe hemorrhage from the operative site kept him there a matter of four hours. Attempts during that time to control the hemorrhage were of doubtful success. The patient was returned to the ward with a Breeke bag held in place by two pounds of traction, and 1000 cc. of fresh whole blood was transfused almost immediately. At 3 o'clock that afternoon the patient perspired profusely, had tachycardia of 120 per minute, blood pressure of 215/105, and had developed a pulsus alternans. Atropin was continued and papaverine, aminophylline, and oxygen therapy were initiated. At 11:30 that night the pulsus alternans had disappeared but frequent premature ventricular systoles had developed. Through the following two days, November 3 and 4, the general condition seemed much improved and the blood pressure and pulse had returned to the patient's usual. At 6 a.m., November 5, he suddenly lost consciousness and became apneic and cyanotic. Caffeine and artificial respiration were administered. Upon recovering consciousness, the patient insisted no pain had preceded the episode. Another such episode developed at 5 p.m. the same day, again with prompt recovery. The blood pressure at the time was 150/90. Half a hour later, death came in such an episode.

An electrocardiogram taken immediately after the 6 a.m. episode revealed frequent runs of ventricular tachycardia, frequent premature ventricular systoles, a flat T-1, low T-2, and deeply inverted T-4. Myocardial infarction and pulmonary embolus were considered complicating possibilities.

Clinical Diagnoses: 1. Prostate, hyperthrophy of, benign, chronic, severe, cause undetermined; 2. Arteriosclerosis, generalized, severe; 3. Infarction, myocardial, acute, secondary to postoperative hemorrhage and "2".

Anatomic Diagnoses: 1. Periarteritis Nodosa, generalized, severe. (Lesions of all stages or ages present); 2. Hemorrhage, postoperative, severe, secondary to "1"; 3. Cardiac arrythmias, various, and probably terminal ventricular fibrillation; 4. Arteriosclerosis, generalized, mild.



CASE No. 4.—Liver. Fibrotic portal area showing small hepatic artery with eosinophilic degeneration of wall, and almost complete fibrotic obliteration of lumen of two other arteries.

COMMENT

Complete gross and microscopic autopsies were performed on all four cases. To list all the anatomic changes would serve too little purpose to justify the consumption of the space required. Some of the laboratory reports are omitted as well and for the same reason.

The patients in all four of these cases had been vaccinated against yellow fever in February or March, 1942; three of them definitely, and the fourth probably, developed hepatitis about two to four months thereafter.

The patient in Case Number 4 is known to have received sulfathiazole as a urinary antiseptic about December, 1943, and in view of his longstanding urinary tract problem and the fact he was a physician, it is rather probable that he received sulfonamides at other times. In Case Number 3 the patient received sulfadiazine, not before, but during his terminal illness, under circumstances explained in the case report.

It is of interest that Krupp [6] was the first to suspect periarteritis nodosa in Case Number 1, as a result of the study of urinary sediments. During the course of hospitalization, but after the diagnosis had been made, the patient in Case Number 2 likewise produced characteristic urinary sediments.

Case Number 4, the only one in which the patient's disease was undiagnosed antemortem, presents features worth comment:

1. Surgeons unfortunate enough to enter a case of periarteritis nodosa face the prospect of dealing with intractable hemorrhage and operative wounds very resistant to healing. The protean manifestations of this disorder paint many pictures very alluring to surgical intervention.

2. If this case is not an example of it, it at least should remind physicians and surgeons of the undependability of blood pressure and pulse readings as indications of the presence or degree of hemorrhage. These may change only when shock is advanced, if not irreversible.

3. In view of the history, the various postoperative cardiac arrythmias and electrocardiogram changes, careful postmortem search was made for coronary disease and myocardial infarction. Only focal, chronic, interstitial, and perivascular myocardial fibrosis was found. Scherf and Klotz,[15] in 1944, reported QRS, ST, or T changes in electrocardiograms of 14 of 15 cases of gastric hemorrhage. The changes seemed, in most cases, unaccompanied by evidence of shock or severe anemia. The electrocardiogram changes returned to normal in two to ten days.

SUMMARY

1. Four hitherto unreported, fatal proven cases of periarteritis are reported.

2. The patients in all four cases were Army officers who had been vaccinated against yellow fever in February or March, 1942. Three of these officers are known to have developed postvaccinal hepatitis; the fourth is believed to have developed it.

3. All four patients died at a single medical installation over a period of 26 months between September, 1942, and November, 1944, their deaths composing two per cent of the total deaths for that period.

4. The medico-surgical profession is reminded that the rapid acceleration of the rate and number of cases of periarteritis nodosa reported may be due, in part, to the induction of cases by the administration of various substances including sulfonamides, serums, tissue extracts and vaccines including yellow fever vaccine.

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